



**UNITED STATES ENVIRONMENTAL PROTECTION AGENCY**  
WASHINGTON, D.C. 20460

OFFICE OF  
PREVENTION, PESTICIDES  
AND TOXIC SUBSTANCES

**Note to Reader**

**Background:** As part of its effort to involve the public in the implementation of the Food Quality Protection Act of 1996 (FQPA), which is designed to ensure that the United States continues to have the safest and most abundant food supply. EPA is undertaking an effort to open public dockets on the organophosphate pesticides. These dockets will make available to all interested parties documents that were developed as part of the U.S. Environmental Protection Agency's process for making reregistration eligibility decisions and tolerance reassessments consistent with FQPA. The dockets include preliminary health assessments and, where available, ecological risk assessments conducted by EPA, rebuttals or corrections to the risk assessments submitted by chemical registrants, and the Agency's response to the registrants' submissions.

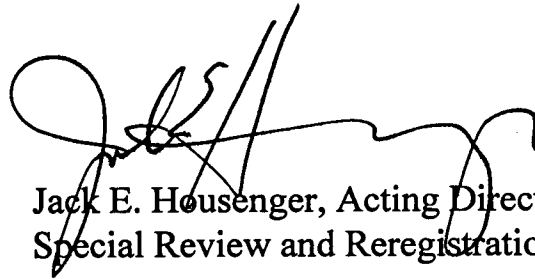
The analyses contained in this docket are preliminary in nature and represent the information available to EPA at the time they were prepared. Additional information may have been submitted to EPA which has not yet been incorporated into these analyses, and registrants or others may be developing relevant information. It's common and appropriate that new information and analyses will be used to revise and refine the evaluations contained in these dockets to make them more comprehensive and realistic. The Agency cautions against premature conclusions based on these preliminary assessments and against any use of information contained in these documents out of their full context. Throughout this process, If unacceptable risks are identified, EPA will act to reduce or eliminate the risks.

There is a 60 day comment period in which the public and all interested parties are invited to submit comments on the information in this docket. Comments should directly relate to this organophosphate and to the information and issues available in the information docket. Once the comment period closes, EPA will review all comments and revise the risk assessments, as necessary.

These preliminary risk assessments represent an early stage in the process by which EPA is evaluating the regulatory requirements applicable to existing pesticides. Through this opportunity for notice and comment, the Agency hopes to advance the openness and scientific soundness underpinning its decisions. This process is designed to assure that America continues to enjoy the safest and most abundant food supply. Through implementation of EPA's tolerance reassessment program under the Food Quality Protection Act, the food supply will become even safer. Leading health experts recommend that all people eat a wide variety of foods, including at least five servings of fruits and vegetables a day.

**Note:** This sheet is provided to help the reader understand how refined and developed the pesticide file is as of the date prepared, what if any changes have occurred recently, and what new information, if any, is expected to be included in the analysis before decisions are made. **It is not meant to be a summary of all current information regarding the chemical.** Rather, the sheet provides some context to better understand the substantive material in the docket ( RED chapters, registrant rebuttals, Agency responses to rebuttals, etc.) for this pesticide.

Further, in some cases, differences may be noted between the RED chapters and the Agency's comprehensive reports on the hazard identification information and safety factors for all organophosphates. In these cases, information in the comprehensive reports is the most current and will, barring the submission of more data that the Agency finds useful, be used in the risk assessments.

A handwritten signature in black ink, appearing to read 'J. Housenger', is written over the typed name and title.

Jack E. Housenger, Acting Director  
Special Review and Reregistration Division

HED DOC. NO. 014115

This report is issued to correct numerical errors (dose levels from the 2-year chronic toxicity/carcinogenicity study in rats) cited in the November 1, 1999 report of the HIARC.

**DATE:** April 26, 2000

**MEMORANDUM**

**SUBJECT:** *CORRECTION to November 1, 1999 MALATHION: Revised NOAEL for Derivation of the Chronic Reference Dose* - Report of the Hazard Identification Assessment Review Committee.

**FROM:** Jess Rowland, Co-Chair  
Hazard Identification Assessment Review Committee  
Health Effects Division (7509C)

**TO:** Paula Deschamp  
Risk Assessor  
Reregistration Branch II  
Health Effects Division (7509C)

**PC Code:** 057701

On October 28, 1999, the Health Effects Division's Hazard Identification Assessment Review Committee (HIARC) evaluated the mean compound intake in the combined chronic toxicity/carcinogenicity study in rats (MRID No. 43942901) and its impact on the derivation of the chronic Reference Dose. The Committee's conclusions are presented in this report.

## Committee Members in Attendance

Members present: David Anderson, William Burnam, Pamela Hurley, Mike Ioannou, Tina Levine, Susan Makris, Nicole Paquette, Jess Rowland, and PV Shah.

Data were presented by Brian Dementi of Toxicology Branch.

### **I. BACKGROUND**

On November 6, 1997, the Hazard Identification Assessment Review Committee (HIARC) selected the NOAEL of 50 ppm for derivation of the chronic Reference Dose (RfD) from the combined chronic toxicity/ carcinogenicity study in rats. The NOAEL was based on inhibition of plasma cholinesterase activity in males at 24 months at 100 ppm (LOAEL) [HIARC Report dated December 17, 1997; HED Document No. 012440].

In the subject study, groups of Fischer 344 rats (90/sex/dose) were fed diets containing Malathion (96.4%; mean purity 97.1%) at 0, 100/50, 500, 6000 or 12000 ppm for up to 24 months. The low dose of 100 ppm was reduced to 50 ppm after 3 months due to inhibition of erythrocyte cholinesterase activity in females. The Data Evaluation Record (DER) of this study presented the mean test substance intake (mg/kg/day) as 4 mg/kg/day for the NOAEL of 50 ppm and as 29 mg/kg/day for the LOAEL of 500 ppm.

The chronic RfD of 0.04 mg/kg/day was derived based on the NOAEL of 4 mg/kg/day and the Uncertainty Factor of 100.

Since that HIARC meeting, the mean compound intake data was reevaluated because of the changes in the dose levels administered during the course of this study (i.e., 100 ppm for 1 to 16 weeks and 50 ppm for 18 to 102 weeks). This data was submitted to the HIARC for evaluation on October 28, 1999.

### **II. REEVALUATION OF THE MEAN TEST SUBSTANCE INTAKE**

The mean test substance intake for rats of both sexes at all doses has been recalculated using periodic test substance intake data from Table G-85 (pp. 482-493 of the study report, MRID 43942901).

These calculations confirm that test compound intakes are actually somewhat lower than those cited in the DER from the study report. As explained in the study report, the larger numbers are attributable to disproportionately greater weight having been given to mean values for the first 16 weeks than to those for the remaining 86 weeks of the 102 week study.

The table of original mean test substance intake values as it appeared on page 29 of the DER is presented in the following table with the newly calculated values in parentheses:

Treatment Group	Mean Test Substance Intake Values (mg/kg/day)			
	Dose Level (ppm)	Weeks	Male (Revised)	Female (Revised)
I	0	1-102	0	0
II	100	1-16	7(7.02)	8(8.15)
	50	18-102	2(2.37)	3(2.95)
	100/50	1-102	4(3.10)	5(3.77)
III	500	1-102	29(26)	35(32)
IV	6000	1-102	359(327)	415(386)
V	12000	1-102	739(677)	868(817)

As the table illustrates, 50 ppm (NOAEL) administered for weeks 18-102 converts to 2.37 mg/kg/day for males and 2.95 mg/kg/day for females. Thus, 500 ppm (LOAEL) is equal to 26 mg/kg/day for males and 32 mg/kg/day for females.

Based on the data in the table above, the NOAEL at 50 ppm should then be converted to 2.37 mg/kg/day for males and to 2.95 mg/kg/day for females (as opposed to 4 mg/kg/day and 5 mg/kg/day reported in the December 17, 1997 HIARC report).

Therefore, the RfD should be revised to 0.024 mg/kg/day based on the NOAEL of 2.4 mg/kg/day (rounded to 2 significant figures) and the U.F. of 100 (as opposed to 0.04 mg/kg/day based on the NOAEL of 4 mg/kg/day and the U.F. of 100 reported in the December 17, 1997 HIARC report).

### III. CONCLUSIONS

The HIARC concluded that the following revisions should be made:

1. The DER should be amended to reflect that the NOAEL of 50 ppm is equal to 2.37 mg/kg/day for males and 2.95 mg/kg/day for females.
2. The chronic RfD should be based on the NOAEL of 2.4 mg/kg/day and the UF of 100, yielding a chronic RfD of 0.024 mg/kg/day.